

### REMARKS

#### Replacement Form PTO-1449

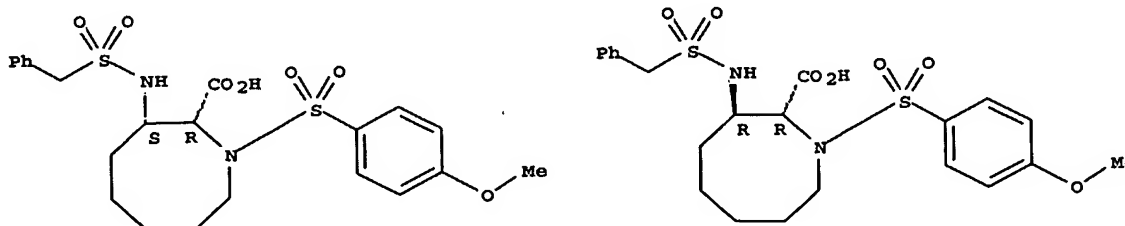
Applicants' representative has identified typographical errors on the Form PTO-1449 that was submitted with the application as filed and, with apologies for the inconvenience, has provided a replacement Form PTO-1449 indicating the correct citations for references C4 and C6 – C8. The Examiner is respectfully requested to replace the previously submitted Form PTO-1449 with the corrected form, or to correct the previously submitted Form PTO-1449, or to submit a Form PTO-892 noting the following correct citations (changes indicated in boldface):

C4	Baldwin <i>et al.</i> , Tetrahedron, 45(19): 6309 (1989), "Non-Proteinogenic Amino Acid Synthesis"
C6	Ninomiya <i>et al.</i> , Tetrahedron, 30: <b>2151</b> (1974), "Phosphorus in Organic Synthesis-VIII"
C7	Wadsworth, Organic Reactions, 25: 73-253 (1977), Chapter 2, "Organic Reactions"
C8	Rabjohn, Organic Reactions, 24: 261-415 (1976), Chapter 4, "Organic Reactions"

#### Amendments to the Claims

Claims 1 and 12 have been amended; these amendments find support in the claims as originally filed and throughout the specification; no new matter has been added.

Claim 1 has been amended to correct a typographical error in line 2 of the claim, and to specify that m is 1 and n is 2. Claim 12 has been amended to recite compounds encompassed within the scope of claim 1 as amended; these compounds are described at page 28, lines 29-32 of the specification. Alternative names for these compounds are provided at page 30, lines 13-16, of the specification, and the Examiner is respectfully requested to note that the Chemical Abstracts Service of the American Chemical Society has provided Registry numbers 228420-43-7 and 228420-44-8 for these compounds, based on the publication (WO 99/32452 A1) of the International Application corresponding to the present application. The structures of these compounds are represented below:



Double Patenting

Claims 1-21 were rejected under the judicially created doctrine of double-patenting, as being unpatentable over the claims of issued U.S. Patent Nos. 6,291,450, 6,335,329, and 6,593,351. Although Applicants do not accede to the basis for the rejection, the amendment to Claim 1 renders the basis for the rejection moot. Claim 1 has been amended to specify the variables presented in Claim 1 so that m is 1 and n is 2, and thus the claims are drawn to 8-membered heterocycles, while the claims of the issued patents cited above are drawn to 6- or 7-membered heterocycles.

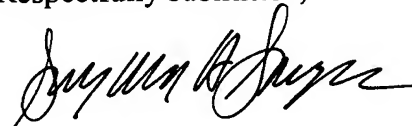
For at least these reasons, withdrawal of the rejection of claims 1-21 on the basis of double-patenting is respectfully requested.

Improper Markush Group

Claims 1-21 were rejected as being drawn to an improper Markush group. Although Applicants do not accede to the grounds for the rejection, the amendment to Claim 1 discussed above overcomes the basis for the rejection, by limiting the compounds of the claims to 8-membered heterocycles (i.e. those where m is 1 and n is 2 in the formula of Claim 1). Therefore, withdrawal of the rejection of claims 1-21 as improper Markush claims is respectfully requested.

If a telephone interview would be helpful in advancing the prosecution of this application, Applicants' attorney invites the Examiner to contact her at the number provided below.

Respectfully submitted,



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Modified Form PTO-1449

Atty. Docket No.

A-509C

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10/601,975

Applicant

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Filing Date

June 23, 2003

Group

1624

## LIST OF REFERENCES CITED BY APPLICANT

(Use several sheets if necessary)

## U.S. PATENT DOCUMENTS

EXAMINER'S INITIALS	DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE IF APPROPRIATE

## FOREIGN PATENT DOCUMENTS

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION YES	NO
B1	EP 606046	7/13/94	EP			X	
B2	EP 803505	10/29/97	EP				X
B3	EP 039051	7/24/85	EP			X	
B4	WO 96/33172	10/24/96	WO			X	
B5	WO 97/18194	5/22/97	WO			X	
B6	WO 96/29313	9/26/96	WO				X

## OTHER DOCUMENTS (Including Publisher, Author, Title, Date, Pertinent Pages, Etc.)

C1	Gibson <i>et al.</i> , J Org. Chem., 59:3216 (1994), "Selective Removal of an N-Boc Protecting Group in the Presence of tert-Butyl Ester and Other Acid-Sensitive Groups"
C2	Svensson <i>et al.</i> , Drug Metabolism r Reviews, 19(2), 165-194 (1988), "The Design and Bioactivation of Presystemically Stable Prodrugs"
C3	Bundgaard, J. Med. Chem., 32(12), 2503 (1989), "A Novel Solution-Stable, Water-Soluble Prodrug Type for Drugs Containing a Hydroxyl or an NH-Acidic Group"
C4	Baldwin <i>et al.</i> , Tetrahedron, 45(19), 6309 (1989), "Non-Proteinogenic Amino Acid Synthesis"
C5	Schuster <i>et al.</i> , Angew. Chem Inst. Ed. Engel, 36: 2036-2056 (1997), "Olefin Metathesis in Organic Chemistry"
C6	Ninomiya <i>et al.</i> , Tetrahedron, 30: 2151 (1974), "Phosphorus in Organic Synthesis-VIII"
C7	Wadsworth, Organic Reactions, 25: 73-253 (1977), Chapter 2, "Organic Reactions"
C8	Rabjohn, Organic Reactions, 24: 261-415 (1976), Chapter 4, "Organic Reactions"
C9	Nagasawa <i>et al.</i> , J. Med. Chem., 14(6), 501-508 (1971), "Medium Ring Homologs of Proline as Potential Amino Acid Antimetabolites"

EXAMINER:

Date Considered:

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.